INTRODUCTION

Backache is a common problem, affecting 80% people at least once in lifetime.\(^1\) Being the fifth most common reason for all physician visits in United States,\(^2\) it affects people belonging to diverse age groups and has strong financial implications on healthcare systems as well as on societies. It can be acute, subacute or chronic. Chronic cases are at times associated with significant disability having non-financial repercussions as well. While a cause is evident in a large proportion of patients, a significant percentage are classified as having idiopathic disease. A few of them may be harbouring rare etiologies not clearly evident at the time of initial presentation. Alkaptonuria, a rare inborn error of metabolism, is one such disease.

We describe a case of alkaptonuria who was diagnosed late in the course of the disease, followed by a discussion on the subject.

CASE REPORT

A 55 years old gentleman reported to our hospital with 15 years history of progressively worsening generalized backache. The pain was more marked in the lower spine, was aggravated by movement, never radiated down the legs and was not accompanied by pain in any other joint of the body. He had recently started feeling difficulty in walking due to pain and stiffness in the back and had started using two sticks to support himself. He had also noticed darkening of his facial skin and rash over his hands worsening over the years. There was no history of any trauma to the back, fever, weakness in the legs or any problems with micturition or defecation. He had never had renal colic or haematuria. The patient was living a retired life after having served in Pakistan Army for 18 years. He was the eldest of three siblings. His brother (8 years younger to him) has a similar skin pigmentation and backache that has developed over the recent years.

On examination, the patient had a macular and hyperkeratotic papular bluish black discolouration of skin over the face and hands (Figure 1). The same figure shows Osler spots visible over both sclera. Pinna of both the ears were hardened. The patient stooped forwards while standing (kyphosis) and could only walk with the support of two sticks. Spine was non-tender but the range of movement as assessed by Schober's test was reduced. Auscultation of the heart did not reveal any murmurs. X-rays of lumbosacral spine (Figure 2) revealed calcification of intervertebral discs. Radiolucent renal stone was also visible on the right side, which was confirmed on ultrasound. Freshly passed urine was normal in colour but darkened within hours when left exposed to air. Complete blood counts, serum calcium, phosphate and alkaline phosphatase were normal. Chest X-ray revealed a normal sized and shaped cardiac shadow without any calcification. Further biochemical testing was not done since the diagnosis was quite evident. Analgesia and physiotherapy was advised.

Backache Due to Alkaptonuria in a Middle Aged Man
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ABSTRACT

Alkaptonuria is a rare cause of backache. A 55 years old gentleman, a retired army personal had been having pain and stiffness in the spine for the last 15 years, accompanied by bluish black discoloration of face and hands. Kyphosis and reduced movement of spine were present. Other joints were spared. Osler spots were visible on the sclera. X-rays revealed calcification of intervertebral discs. Asymptomatic renal stone was identified. There was no cardiac involvement. Symptomatic care was provided.

Key Words: Alkaptonuria, Backache, Arthritis, Kyphosis, Intervertebral disc calcification, Dark urine, Urolithiasis, Osler spots.
The brother did not come to the clinic for evaluation despite repeated requests. However, his sister is apparently normal.

**DISCUSSION**

Alkaptonuria is a rare autosomal recessive metabolic disorder occurring in 1 out of every 250000 live births. Characterized by deficiency of homogentisic acid oxidase, it results in impaired phenylalanine and tyrosine metabolism, leading to increased urinary homogentesic acid (HGA) excretion and accumulation of oxidized HGA pigment in various collagenous tissues of the body.

Most of the patients are asymptomatic in the young age. Darkening of urine on standing is usually the first manifestation that results from oxidation and polymerization of HGA. Since this process is dependent on urine pH, some patients with acidic urine may never notice this change. Bluish black pigmentation, generally found in the skin, sclera and buccal mucosa, starts in the fourth/fifth decade. The term ochronosis is attributed to its yellow microscopic appearance. Arthritis is the most disabling symptom, behaving clinically as ankylosing spondylitis. It affects the spine and peripheral large joints, characteristically sparing the sacroiliac joints. Pigment stones resulting from high urinary homogentisic acid are common. Calcification can be seen in prostate and coronary arteries. Other cardiac manifestations include aortic and mitral valvulitis.

The diagnosis is confirmed by measurement of HGA by enzymatic spectrophotometry, gas liquid chromatography or high-pressure liquid chromatography. We did not get any of these done, since the patient had florid manifestations and there was no diagnostic uncertainty on clinical grounds. Currently, treatment for alkaptonuria is totally palliative, revolving around lifestyle changes, effective analgesia and physiotherapy. Dietary restriction of phenylalanine and tyrosine is not helpful because of poor long-term compliance. Similarly, the use of vitamin C in high doses has been advocated but clinical trials confirming efficacy are lacking. A recent study has proved that the combination of N-acetyl cysteine with ascorbic acid is a more effective treatment option. The same study also highlighted the role of antioxidants like taurine, phytic acid, ferulic acid and lipoic acid in reducing the production of ochronotic pigment and protein oxidation.

Another agent that has received much attention over the last few years is nitisinone, an inhibitor of the enzyme 4-hydroxyphenylpyruvate dioxygenase. This enzyme converts 4-hydroxyphenylpyruvate to homogentisic acid. A 95% reduction in urine and plasma HGA levels over a period of 3 years was demonstrated in a clinical trial, though the clinical parameters did not improve. Long-term side effects of this drug are still unknown.

**REFERENCES**